

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference MXI-166PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 01/ 15114	International filing date (day/month/year) 08/05/2001	(Earliest) Priority Date (day/month/year) 08/05/2000
Applicant MEDAREX, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/15114

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C07K16/28	C12N5/20	A01K67/027	C07K16/46	A61K39/395
	A61K47/48	G01N33/569	G01N33/577	C12N15/63	A61K39/00
	A61K39/02	A61K39/12	A61P31/00	A61P35/00	A61P37/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

PAJ, EPO-Internal, WPI Data, BIOSIS, EMBL, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 876 917 A (HART DEREK N J) 2 March 1999 (1999-03-02) column 2, line 33 -column 3, line 56 ---	1-55
X	WO 98 15579 A (CANTERBURY HEALTH LIMITED ;HART DEREK NIGEL JOHN (NZ)) 16 April 1998 (1998-04-16) page 2, line 5 -page 3, line 17 page 12, line 25 -page 16, line 4 ---	1-55
X	WO 95 15340 A (UNIV LELAND STANFORD JUNIOR) 8 June 1995 (1995-06-08) page 4, line 12 -page 5, line 7 page 10, line 1 -page 14, line 26; claims 1-10 --- -/--	1-55

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

S document member of the same patent family

Date of the actual completion of the international search

13 May 2002

Date of mailing of the international search report

23/05/2002

Name and mailing address of the ISA

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Authorized officer

Muller, K

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/15114

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE MEDLINE 'Online! January 1997 (1997-01) NOORMAN F ET AL: "Monoclonal antibodies against the human mannose receptor as a specific marker in flow cytometry and immunohistochemistry for macrophages." Database accession no. NLM9000538 XP002198703 abstract & JOURNAL OF LEUKOCYTE BIOLOGY. UNITED STATES JAN 1997, vol. 61, no. 1, January 1997 (1997-01), pages 63-72, ISSN: 0741-5400 ---	1-55
P,X	WO 00 63251 A (UNIV NIJMEGEN ;TORENSMA RUURD (NL); FIGDOR CARL GUSTAV (NL); GEIJT) 26 October 2000 (2000-10-26) page 8, line 25 -page 14, line 22 claims 1-26 ---	1-55
A	US 5 922 845 A (KELER TIBOR ET AL) 13 July 1999 (1999-07-13) the whole document ---	17-19
A	WO 99 55369 A (SMITHKLINE BEECHAM CORP ;TAYLOR ALEXANDER H (US)) 4 November 1999 (1999-11-04) page 46 page 66; examples 1,2 -----	51

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: Part of claims 1-55

In view of the large number and also the wording of the claims presently on file (55 claims including 26 independent claims of which 14 are product claims, 11 are method claims and one relates to a "transgenic animal"), which render it difficult, if not impossible, to determine the matter for which protection is sought, the present application fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful search is impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and concise), namely those parts of claims 1-55 which involve an monoclonal antibody that specifically binds to dendritic cells and has a binding affinity constant to a dendritic cell as defined in feature a) of claim 1. In addition also the more precisely defined claim 51, furthermore comprising the sequences 1 and 2, as well as claim 52 relating to a defined epitope on the dendritic cells, have been searched. The further numerous characteristics defining the claimed products (antibodies) are either mainly defined in terms of the effect to be achieved without any indication of concrete technical features which would allow to determine how the said effect is achieved and/or are defined in different terms which are either not related to said (searched) characteristics or even inconsistent with one another. See for instance the (unrelated) functional features b) to c) of claim 1 claimed per se in some of the independent claims. Furthermore see also claim 1, d) in which the claimed antibody should have the ability to activate dendritic cells, whereas in claim 10 (for example) it should inhibit the growth of dendritic cells. In claim 17 the claimed product is not even limited to any of the separate characteristics of claim 1 (or 51 or 52) but relates to a bispecific molecule comprising a first binding specificity for dendritic cells and a second binding specificity for an Fc receptor. The same remark is true for the "molecular complex" in claim 33 which only has a specificity for a component on the surface of a dendritic cell and at least one antigen "linked to said binding specificity" which is again defined in terms of the effect to be achieved. In claim 43, the claimed "bispecific" molecule is defined in yet another way, whereby the second specificity now relates to a target cell ranging from tumour cells to microbial pathogens etc. It should be noted that the list of the above-mentioned unsearched possibilities covered by the scope of the present claims 1-55 is not exhaustive and only represents selected examples to support the lack of clarity and support objection underlying the present incomplete search. The lack of clarity objection not only relates to the "functional definitions" but also to the use of unclear and undefined terms (see for example the arbitrary hybridoma designations of claim 7,14,34).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/15114

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 23-29, 32, 38-42, 53 and 54 (those parts of the claims relating to an in vivo method) are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: Part of claims 1-55
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/15114

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5876917	A	02-03-1999	AU 8068694 A	23-05-1995
			WO 9512409 A1	11-05-1995
WO 9815579	A	16-04-1998	AU 744637 B2	28-02-2002
			AU 4639397 A	05-05-1998
			EP 0956304 A1	17-11-1999
			JP 2001502670 T	27-02-2001
			WO 9815579 A1	16-04-1998
			NZ 335545 A	26-01-2001
WO 9515340	A	08-06-1995	WO 9515340 A1	08-06-1995
WO 0063251	A	26-10-2000	EP 1046651 A1	25-10-2000
			AU 4152600 A	02-11-2000
			EP 1086137 A1	28-03-2001
			WO 0063251 A1	26-10-2000
US 5922845	A	13-07-1999	AU 705643 B2	27-05-1999
			AU 3723397 A	09-02-1998
			CA 2259371 A1	22-01-1998
			CN 1230198 A	29-09-1999
			EP 0914346 A1	12-05-1999
			HU 9903951 A2	28-03-2000
			JP 2000505091 T	25-04-2000
			PL 331091 A1	21-06-1999
			WO 9802463 A1	22-01-1998
			US 6303755 B1	16-10-2001
			US 2001014328 A1	16-08-2001
			US 6193966 B1	27-02-2001
WO 9955369	A	04-11-1999	CA 2327505 A1	04-11-1999
			EP 1073464 A1	07-02-2001
			WO 9955369 A1	04-11-1999

PATENT COOPERATION TREATY

RKN

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

REMILLARD, Jane E.
Lahive & Cockfield, LLP
28 State Street
Boston, MA 02109
ETATS-UNIS D'AMERIQUE

WRITTEN OPINION

(PCT Rule 66)

6 DAY notice - July 9, 2002
Written opinion due - July 14, 2002

Date of mailing
(day/month/year) 14/06/2002

Applicant's or agent's file reference
MXI-166PC

REPLY DUE
within 1/00 months/days
from the above date of mailing

International application No.

PCT/US 01/ 15114

International filing date (day/month/year)

08/05/2001

Priority date (day/month/year)

08/05/2000

International Patent Classification (IPC) or both national classification and IPC

C07K16/28

Applicant

MEDAREX, INC. et al.

1. This written opinion is the first drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 08/09/2002

Name and mailing address of the IPEA/



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Authorized officer
Examiner

Formalities officer
(incl. extension of time limits)
Tel. (+49-89) 2399 2828

ENTERED

RECEIVED
LAHIVE & COCKFIELD
DOCKET

JUN 18 2002

RETRIEVED:
FORWARDED:

I. Basis of the opinion

The basis of this written opinion is the application as originally filed.

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question of whether the claimed invention appears to be novel, to involve an inventive step, or to be industrially applicable has not been and will not be the subject of the international preliminary examination in respect of the claims which have not been searched (Article 17(2)(a) or (3) and Rule 66.1(e) PCT; see also international search report).

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability

1. To the extent that the international preliminary examination has been carried out (see item III above), the following is pointed out:
2. In light of the documents cited in the international search report, it is considered that the invention as defined in at least some of the claims, which have been the subject of an international search report, does not appear to meet the criteria mentioned in Article 33(1) PCT, i.e. does not appear to be novel and/or to involve an inventive step (see international search report, in particular the documents cited X and/or Y and corresponding claim references).
3. If amendments are filed, the applicant should comply with the requirements of Rule 66.8 PCT and indicate the basis of the amendments in the documents of the application as originally filed (Article 34 (2) (b) PCT) otherwise these amendments may not be taken into consideration for the establishment of the international preliminary examination report. The attention of the applicant is drawn to the fact that if the application contains an unnecessary plurality of independent claims, no examination of any of the claims will be carried out.

NB: Should the applicant decide to request detailed substantive examination, then an international preliminary examination report will normally be established directly. Exceptionally the examiner may draw up a second written opinion, should this be explicitly requested.